REMARKS

By the present amendment, Applicant has submitted a substitute specification, cancel the original claim and added Claims 2-15, which remain pending in the present application. Claim 1 is an independent claim.

In the recent Office Action the Examiner objected to the abstract of the disclosure, the specification and claim because of certain informalities. Claim 1 was also rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Claim 1 was further rejected by the Examiner under 35 U.S.C. § 102(b) as being anticipated by Bonte (U.S. Patent No. 5,770,223), and under 35 U.S.C. § 102(e) as being anticipated by Wollfson et al. (U.S. Patent No. 6,534,527).

The Examiner noted that the abstract and specification are difficult to read because of errors and "bleeding" of the text. In this regard, Applicant has amended the abstract of the disclosure to correct the noted errors . Reproducing the amended abstract should serve to facilitate its reading. Also, Applicant submits herewith a substitute specification in compliance with 37 CFR § 1.125 since the legibility of the original application papers renders it difficult to read. A marked-up version of the specification is also submitted showing all the changes relative to the original version of the specification. Care has been exercised to ensure that the substitute specification includes no new matter.

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With regard to the Examiner's rejection of Claim 1 under Section 112, second paragraph, the cancellation of the instant claim by the present amendment should serve to obviate this particular ground of rejection. Applicant submits that the newly introduced claims are substantially devoid of the language criticized of record by the Examiner. However, Applicant traverses the Examiner's assertion that the terminology "a trace amount" (as now recited in Claim 4) "is vague and is not described in the specification." The original specification at page 7, lines 9-13, clearly sets forth that the compositions of the present invention may be formulated to contain some nicotine "in quantities substantially less than the naturally occurring nicotine agonist alkaloids." Thus, one skilled in the art would be readily apprised from Applicant's written description of the relatively minor amounts of nicotine present in the claimed compositions. Applicant respectfully submits that new independent Claim 2 and corresponding dependent Claims 3-15 are sufficiently supported by the specification and are believed to be in full compliance with the requirements of 35 U.S.C. 112, second paragraph.

Regarding the grounds of rejection based on prior art, Applicant will advance arguments hereinbelow to illustrate the manner in which the invention defined by the newly introduced claims is patentably distinguishable from the cited and applied prior art. Reconsideration of the present application is respectfully requested.

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New independent Claim 2 sets forth a composition for relieving withdrawal symptoms and craving in a nicotine dependent or nicotine habituated person who is abstaining from or reducing nicotine intake. The claimed composition is defined as comprising a herbal component providing a naturally occurring nicotine agonist, wherein the nicotine agonist includes at least anabasine in an amount of at least about 0.1 weight percent of the herbal component, and a carrier for the herbal component. The carrier is further characterized as being formulated for oral mucosal absorption. New dependent Claim 3 further includes an effective amount of anatabine, and dependent Claim 4 optionally includes nicotine in amounts of from about 0 weight percent nicotine to trace amounts. Dependent Claim 5 sets forth that the herbal component is obtained from a Markush grouping of particular plants, and Claim 6 is limited to a specific plant. New dependent Claim 7 states that the carrier is formulated into a dosage unit of selected forms. Claims 8 and 9 specifies that the dosage unit contains about 5 mg to about 600 mg dry weight and liquid extract of the herbal component, respectively. Claims 10-12 set forth the content of anabasine in the dosage unit. New Claim 13 is drawn to the corresponding method of using the composition of Claim 2, and method Claims 14 and 15 specifies the dosage amount of anabasine administered on a daily basis. No new matter is involved by the newly presented claims since the claimed limitations find clear support in the written description contained in the original specification.

Applicant contends that patent to Bonte et al. is deficient as an anticipatory reference against the present claims. Further, it is Applicant's contention that the instant reference is

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insufficient to render the presently claimed invention obvious within the meaning of 35 U.S.C. 103. In this regard, the Bonte et al. patent essentially discloses the use of *Medicago saponins*, or a plant extract in which it is present, for the preparation of dermatological compositions. This reference teaches that the corresponding saponin or extract thereof is incorporated into a hydrated lipidic lamellar phase or into liposomes. The compositions taught by Bonte et al. are applied topically, and are stated to be useful for promoting renewal of the epidermis, stimulating hair regrowth or delaying hair loss, for example. In contrast, Applicant's herbal compositions are orally administered and possess therapeutic properties completely unrelated to those taught by the patent to Bonte et al.

Applicant contends that the patent to Bonte et al. fails to realistically teach or reasonably suggest Applicant's presently claimed compositions and corresponding method of use. Moreover, it is Applicant's contention that one of ordinary skill in the art, furnished only with the realistic teachings afforded by this reference and without the benefit of Applicant's own disclosure, would not be capable of arriving at the invention defined by the present claims. For at least these reasons, Applicant respectfully submits that independent Claims 2 and and corresponding dependent Claims 3-15 are allowable over the prior art of record.

With regard to the Examiner's rejection under 35 U.S.C. 102(e) as being anticipated by Wolfson et al., it should first be noted that Phillip Wolfson is a named inventor in U.S. Patent No. 6,534,527 and the present application. The compositions disclosed by the referenced patent

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includes multiple nicotine agonists, one of which is anabasine in an amount of at least 0.2 weight percent. In contrast, the presently claimed composition comprises a herbal component that may provide a single naturally occurring nicotine agonist, wherein the nicotine agonist includes at least anabasine in an amount of at least about 0.1 weight percent of the herbal component. Also, the claimed compositions include a carrier that is formulated to facilitate dispersion and absorption of the nicotine agonist through the mucosal lining of the oral cavity and into the circulation. No mention or suggestion is made in U.S. Patent No. 6,534,527 of this particular feature of the carrier.

In order to show anticipation under 35 U.S.C. 102, the reference must show every element of the claimed invention identically. *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1 USPQ2d 1081 (Fed. Cir. 1986), *Akzo N.V. v. United States Intl. Trade Commission*, 808 F.2d 1471, 1 USPQ2d 1241 (Fed. Cir. 1986). Not only must every element claimed be shown in the prior art reference, but every claimed limitation of each of the elements must be shown; otherwise, the only possible rejection is for obviousness under 35 U.S.C. 103. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984), *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985).

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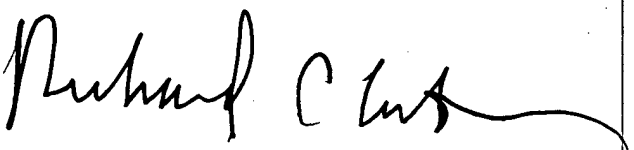
For the foregoing reasons, Applicant respectfully submits that the present application is in condition for allowance. If such is not the case, the Examiner is requested to kindly contact the undersigned in an effort to satisfactorily conclude the prosecution of this application.

Respectfully submitted,



Richard C. Litman
Registration No. 30,868
(703) 486-1000

RCL:dht

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P.O. BOX 15035
ARLINGTON, VA 22215
(703) 486-1000

Application No.:10/611,911
Art Unit: 1654

Attorney Docket No. 19641.06
Confirmation No. 5582

SPECIFICATION WITH MARKINGS SHOWING CHANGES

Attorney Docket No. 19641.06

IN THE APPLICATION

OF

PHILIP E. WOLFSON

FOR A

BUCCAL AND SUBLINGUAL MUCOSALLY ABSORBED HERBAL COMPOSITIONS FOR RELIEVING NICOTINE WITHDRAWAL SYMTOMS AND CRAVING FOR NICOTINE AND NICOTINE CONTAINING SUBSTANCES

BUCCAL AND SUBLINGUAL MUCOSALLY ABSORBED HERBAL COMPOSITIONS FOR RELIEVING NICOTINE WITHDRAWAL SYMTOMS AND CRAVING FOR NICOTINE AND NICOTINE CONTAINING SUBSTANCES

CROSS-REFERENCE TO RELATED APPLICATION

This application claims the benefit of U.S. Provisional Patent Application Serial No. 60/394,157, filed July 5, 2002.

~~BUCCAL and SUBLINGUAL MUCOSALLY ABSORBED HERBAL COMPOSITIONS for RELIEVING NICOTINE WITHDRAWAL SYMTOMS and CRAVING for NICOTINE and NICOTINE CONTAINING SUBSTANCES~~

BACKGROUND OF THE INVENTION

1. FIELD OF THE INVENTION

The present invention generally relates to compositions useful in relieving the symptoms of nicotine withdrawal and craving for nicotine ~~as contained in any and all of the myriads products that contain nicotine, such as cigarettes, cigars, smoking tobacco, chewing tobacco, and products that contain nicotine as a chemical, this~~ in nicotine habituated persons who are abstaining from or reducing nicotine intake, [[;]] and more particularly the invention relates to compositions that are absorbed through the mucosal tissues of the oral cavity and include an herbal component which provides multiple nicotine agonists, one of which is anabasine, but contain little or no nicotine~~; and which are designed to be absorbed through the mucosal tissues of the oral cavity~~.

2. DESCRIPTION OF RELATED ART

Using 1996 data, the prevalence of cigarette smoking in the United States among adults was about 27% or 55 million people. Each year some 30% of smokers try to quit, but only about 10% are successful. The efficacy rate for formal cessation programs, defined as abstinence at one year follow-up, is between 20 and 40% of those enrolled. The most telling fact is that the majority of smokers who are successful in quitting tobacco have done so on their own. In the past ten years, 47.5% of persons attempting to quit smoking on their own were successful compared to 23.6% of those who used smoking cessation programs to quit.

There have been many therapies and pharmacologic agents used to assist in smoking cessation. Nicotine delivered through gum, transdermal patches, and nasal sprays in declining dosages over time have been the principal pharmacologic strategies, i.e., a withdrawal over time minus the tar of actual cigarettes.

More recently the anti-depressant bupropion has been reintroduced in a long acting twice-a-day preparation for smoking cessation. The anxiolytic buspirone has been suggested for use as an adjunct for the treatment of nicotine addiction. These preparations are costly, may have undesirable side effects and require prescriptions and medical supervision.

There have been several herbal preparations suggested for smoking cessation. A lobelia-based preparation was withdrawn because of FDA concerns sparked by toxicity reports from human use. U.S. Patent No. 4,817,640, issued April 4, 1989 to Summers, describes herbal chew and snuff products, which are said to proximate the texture, taste, and organoleptic sensation of a snuff or chew composition. The herbs are selected from dandelion, papaya, dock or sorrel, sunflower, calendula, nasturtium, mallow, chicory, corn silk, and mixtures thereof. In addition, clover is suggested for use, with red clover being the preferred major component for the snuff composition.

Among other smoking cessation products have been chewing gums that include pure anabasine in salt form. Thus, Russian Patent No. 1,268,141, published November 7, 1986, describes an anti-nicotine gum formed by mixing an aqueous anabasine-HCl solution into syrup, and formulating further with a base and sugar. U.S. Patent No. 4,971,079, issued November 20, 1990 to Talapin et al., describes another chewing gum carrier where an alkaloid, preferably anabasine hydrochloride, is coupled via a cation exchange group to a biological absorbable polymeric vehicle, and this coupled composition is then formulated in a chewing gum.

U.S. Patent No. 5,942,244, issued August 24, 1999 to

Friedman et al., describes tablet formulations for local and slow release of herbal medication into the oral cavity of a subject.

Anabasine and other alkaloids, such as anatabine, are structurally similar to nicotine, and are believed to substitute for nicotine (as agonists) at nicotine receptor sites.

SUMMARY OF TBE INVENTION

The present invention consists of compositions useful in relieving craving in nicotine habituated persons who are voluntarily abstaining from or reducing nicotine consumption. The invention consists of an herb or an herbal extract providing one or more naturally occurring nicotine agonists, at least one of the nicotine agonists being anabasine in an amount of at least about 0.1 (1/10th of one percent) weight percent of the herb or herbal extract, the herb or herbal extract having from about 0 weight percent nicotine to trace levels of nicotine therein. The composition further includes carriers (e.g. solid or liquid) for the herb or herbal extract some of which will facilitate dispersion and absorption of these alkaloids -anabasine, anatabine, etc- through the mucosal lining of the oral cavity and into the circulation.

A preferred combination of nicotine agonists is anabasine

and anatabine provided by flowers, dried leaves, stems, and/or roots, particularly of the *Nicotiana glauca* plant, or an herbal extract thereof. Suitable carriers for oral mucosal absorption include gums or binders (particularly for chewing gum formulations), sucking candies, syrups, oral films, intra-oral sprays, sub-lingual liquids, oral fast dissolving tablets for sub-lingual dispersion, micro-emulsions, sublingual buccal effervescents, trans-mucosal delivery systems, lozenge formulations, and any and all delivery systems having the potential for enabling in one form or another the oral adsorption of the active principles, such as anabasine, etc.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Broadly, compositions of this invention are suitably formulated for oral mucosal absorption (e.g., chewing gum, sucking candies, syrups, oral films, intra-oral sprays, sub-lingual liquids, oral fast dissolving tablets for sub-lingual dispersion, micro-emulsions, sublingual buccal effervescents, trans-mucosal delivery systems, lozenge formulations, and the like). Regardless of the particular form, the compositions consist essentially of an herbal component that is derived from a plant or mixtures of plants having a quantity of naturally occurring alkaloid agonists of nicotine such as anabasine, but with little or no nicotine. Among

the plants from which the herbal component may be obtained are, for example, *Medicago sativa*, *Lupinus formosus*, *Solanum carolinense*, *Aniba coto*, *Zinnia elegans*, *Sophora pachycarpa*, *Verbascum songaricum*, *Priestleya elliptica*, *Priestleya tomentosa*, *Haloxylon persicum*, *Haloxylon salicornicum*, and *Nicotiana glauca*. Some species include quantities of both anabasine and nicotine, such as *N. glauca* and *N. debneyi* (with anabasine predominating).

A particularly preferred plant for obtaining the herbal component is *N. glauca* (sometimes commonly called "tree tobacco"). This plant grows wildly in the western United States. It has been medicinally used as an analgesic poultice applied externally. Anabasine is the most prominent of the nicotine like alkaloid in *N. glauca* leaves and other parts of the plant.

The herbal component of this invention will usually be provided by (or derived from) plant foliage (leaves and stems), although plant roots may also be used, since the concentrations of naturally occurring nicotine agonist may vary in the different parts of each respective plant. The herbal component may be prepared as dried plant parts, or any of a variety extracts therefrom. Herbal extracts are extracts of plant materials, such as, for example, a tincture of botanical materials, which typically are prepared by contacting botanical material with a solvent (*British Herbal Pharmacopeia*, Peter R. Bradley, Ed.,

British Herbal Medicine Association, 1983; and *British Herbal Compendium*, Peter R. Bradley, ed., British Herbal Medicine Association, 1992). The solvent, for example, can be aqueous or organic, or a combination thereof. Acceptable organic solvents include, but are not limited to, glycerin, propylene glycol, ethanol or other alcohols, hexane, methylene chloride or a combination thereof. The most preferred solvents are hydro alcoholic solvents as defined in *British Herbal Pharmacopeia and Compendium*. Other extraction methods may be used--such as super-critical carbon dioxide, liquid nitrogen, fractionation, wiped film drying, etc.

Since a smoking cessation program may begin by gradual cessation of nicotine usage, followed by more complete, or by complete cessation of nicotine usage, inventive compositions may be formulated that have some nicotine (albeit in quantities substantially less than the naturally occurring nicotine agonist alkaloids). [[,]] These substances are often used in a program [[of]] in diminishing amounts over time, [[of these substances, these substances]] being absorbed through the oral mucosa, the purpose of this being being to diminish or even eliminate the symptons that occur as a result of nicotine withdrawal, including acute and later cravings for nicotine in its myriad forms, such as cigarettes, cigars, smoking tobacco, chewing tobacco, and

products that contain nicotine as a chemical. Or the same or similar program may be provided using only the naturally occurring nicotine agonist alkaloids, without the presence of any quantity of nicotine; or only trace amounts of nicotine that are not substantially active because of their very small concentrations in the herbal materials being used.

Use of herbs or herbal extracts in accordance with this invention may provide a complex mixture of ingredients. Since an agonist stimulates the receptor by stabilizing an active confirmation, and this stabilization can be achieved in many ways depending upon the chemical nature of the ligand and on the structure of the receptor, the combination of agonists provided from a source of complex ingredients, such as the suitable herbs or herbal extracts of this invention, may achieve a stabilizing function through multiple interactions of different parts of the target receptor, thus reducing nicotine withdrawal symptoms and craving.

In compositions of this invention, focusing on the anabasine content per recommended dose the range of the amount of anabasine is between about 0.2 mg to about 8 mg, more preferably from about 0.5 mg to about 4 mg. Thus, for examle, if a recommended daily dose ranges up to 8 oral films or chewing gum pieces, then a person could be receiving could be receiving from 0.2mg to 64

mg/day, but most preferably between 2-16 mg/day of anabasine contained in a standardized extract.

Compositions of the invention preferably have from only small, or trace, amounts of nicotine or no nicotine at all. Thus, the amount of nicotine per recommended dose will be from 0 wt.% to trace levels (unless a product is formulated with explicit amounts of nicotine plus the herbal component as an aid for nicotine cessation or reduction).

When formulated as lozenges, chewing gums, or other forms discussed above and below, it is contemplated that the herbal component will be present in an amount from about 5 mg to about 600 mg dry weight, or about 5mg to 600 mg liquid extract. Such compositions will typically also include additional components such as a binder, a humectant, and flavoring agents such as sweeteners, artificial or natural fruit flavors, oils, and the like. Coloring may also be included. Different strategies for delivering the active principles will entail different formulations and components specific to those products.

Thus, to give an example, in one embodiment, the composition is included in a chewing gum formulation. The formulations of chewing gum are conventional, and well known to those skilled in the art. For example, a carrier may be provided that may be mixed with the herbal component. Suitable carriers, particularly in

formulating chewing gums, comprise Arabic, guar, and natural rubber gums. Other typical components are sweeteners (sugar, saccharin, sorbitol, aspartame), flavoring agents (e.g., mints, fruits, spices), coloring agents, and the like.

For example, the chewing gum or solid carrier may be composed, in its basic formula, of ingredients such as sucrose, corn syrup, gum base, coloring and flavoring. Ingredients such as HSH (hydrogenated starch hydrolysate), sorbitol, xylitol, and/or isomalt can replace sucrose and corn syrup at different ratios. As an example of preparation, to a hot water jacketed stainless steel gum mixer equipped with sigma tangential blades rotating at 9-12 rpm with a 1:2 rotating ratio, molten gum base may be added at approximately 55-55°C, and corn syrup or HSH, added at room temperature in the desired amounts, and mixed until fully dispersed. When a homogeneous mix is obtained, sucrose or sorbitol, xylitol, or isomalt may be added, all in powder form, and mixed until fully dispersed. During the process of the addition of the powder material, the herbal component may be added. Color, flavoring, and any other ingredient deemed necessary for the particular formula may be added. The gummy mass is then discharged from the gum mixer and conveyed to the gum forming equipment.

Thus, for example, the solid portion or chewing gum used as

a carrier for the herbal component may be composed of sucrose (10-80%, preferably 15-50%), corn syrup (5-60%, preferably 10-30%), gum base (10-90%, preferably 20-80%), sorbitol (10-60%, preferably 20-50%), hydrogenated starch hydrolysate (HSH) (5-60%, preferably 10-30%), hydrolyzed proteins (1-8%, preferably 1.5-3.0%), isomalt (10-80%, preferably 15-50%), xylitol (10-80%, preferably 15-50%), artificial sweeteners (0.2-2.0%, preferably 0.5-1.0%), natural sweeteners, coloring, and flavor ingredients - to appearance and taste. Additional ingredients may include other botanical extracts, gelatin, glycerin, starch and modified starches (1-7%, preferably 1.5-5.0%), these being used for the purpose of modifying texture and chewing properties of the gum as well as to enhance the release of nicotine agonists from the gum matrix. The texture and physical properties of the finished product are affected by the final form of the chewing gum, which can also be in sugar or sugar-free form. Such a chewing gum formulation may also include a liquid center in the gum. In such case, the herbal component, preferably in the form of an herbal extract in suitable solvent, may be incorporated into or serve as the liquid center.

In another embodiment, the herb or herbal extract component of this invention is included in sucking candies, syrups, oral films, intra-oral sprays, sub-lingual liquids, oral fast

dissolving tablets for sub-lingual dispersion, micro-emulsions, sublingual buccal effervescents, trans-mucosal delivery systems, lozenge formulations, all formulated for oral administration of the medication with local effects and absorption in the oral cavity. Known agents, binders, and the like as carriers may be used in such formulations.

Further, liquid preparations (where the carrier is a liquid) and emulsions are also contemplated for the inventive compositions to enable oral mucosal dispersion and absorption.

It is to be understood that while the invention has been described above in conjunction with preferred specific embodiments, the description and examples are intended to illustrate and not limit the scope of the invention.